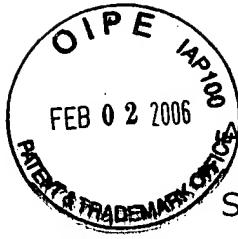


Docket: NEB-177-PUS



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Evans et al.

EXAMINER: Schnizer

SERIAL NO.: 09/937,070

GROUP: 1656

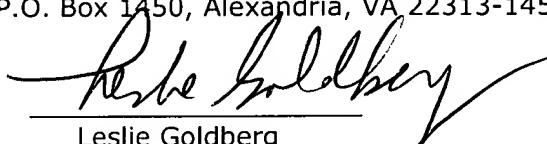
FILED: January 29, 2002

FOR: Method for Producing Circular or Multimeric Protein Species
in vivo or *in vitro* and Related Methods

Mail Stop AF
Commissioner for Patents
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Leslie Goldberg

Sir:

DECLARATION UNDER 37 C.F.R. §1.131

As a below named inventor, I hereby declare that:

1. My name is Dr. Ming Xu, Senior Scientist at New England Biolabs Inc. My resume is attached.
2. The Examiner has rejected claims 12, 14 and 16 in the above application, directed to a method for the *in vivo* production of a cyclic

polypeptide, as invented first by Scott et al. PNAS 96, pp 13638-13643 published November 23, 1999.

3. However, the present claimed invention was invented prior to November, 1999 as recorded in dated pages in my laboratory notebook.

4. I further declare under penalty of perjury pursuant to laws of the United States of America, the foregoing is true and correct.

Dr. Ming Xu

Dr. Ming Xu

Jan. 27th, 2006

Date

Ming-Qun Xu, Ph.D.
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Education:

B.S. 1982 University of Science and Technology of China

Ph.D. 1989 Molecular Biology, Department of Biological Sciences, State University of New York at Albany

Work History

1990-1992: Postdoctoral research on self-splicing introns with Dr. David Shub, SUNY at Albany
Discovered the first eubacterial intron (Xu et al. *Science*, 1990)

1992 – 1994: Postdoctoral research with Dr. Fran Perler at New England Biolabs, Inc. Performed
the first *in vitro* protein splicing experiment (Xu et al., *Cell* 1993)

1994 – 1997: Staff Scientist at New England Biolabs, Inc. Investigated the chemical mechanism
of protein self-splicing. Developed the intein-based affinity purification system –
IMPACT.

1997 – present: Senior Scientist at New England Biolabs, Inc. Structural and mechanistic studies
of self-splicing inteins. Engineered inteins for protein semisynthesis, protein
backbone cyclization and *trans*-splicing.

2001-2005: Managing Director, New England Biolabs (Beijing) Ltd.

Current Research Interest:

Structural and mechanistic studies of protein splicing have been conducted by collaboration
to solve the crystal structures of self-splicing-inteins derived from the *dnaB* and *dnaE* genes of
Synechocystis sp. PCC6803. The finding that the DnaE intein precursor structure contains a zinc
ion, the only identified inhibitor of both *cis*- and *trans*-splicing, chelating the highly conserved
Cys160 and Asp140 reveals the structural basis of Zn²⁺-mediated inhibition. These structural

studies provide insight into the sequential reaction property of protein splicing as well as the strategies to utilize inteins for protein engineering.

A number of intein engineering projects have been carried out for protein/antibody affinity purification, protein labeling and tagging, ligation and cyclization of expressed proteins. The Intein-mediated protein ligation (IPL) method has been applied to new fields including antibody characterization, epitope mapping, kinase/phosphatase assays for analysis via peptide arrays, western blots and ELISA.

PUBLICATIONS:

1. Ming-Qun Xu, Inca Ghosh, Samvel Kochinyan and Luo Sun. Intein-mediated Peptide Arrays for Epitope Mapping and Kinase/Phosphatase Assays. *Methods in Molecular Biology*, vol., *Microarrays: Methods and Protocols Edited by J.B. Rampal. Humana Press Inc., Totowa, NY. In press.*
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